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10/560,422	05/03/2006	Mats Ranby	RANB3002/REF	5307

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EXAMINER	
WALLENHORST, MAUREEN	
ART UNIT	PAPER NUMBER
1797	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,422	RANBY, MATS	
	Examiner	Art Unit	
	Maureen M. Wallenhorst	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-7 and 9-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-7 and 9-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

2. Claims 1-3, 5-7, 9-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In part b) of claim 1, the phrase "the mixture" lacks antecedent basis. In order for this phrase to have proper antecedent basis, it is suggested to insert the phrase --to form a mixture-- in part a) of claim 1 after the phrase "a defined volume of a liquid reagent".

On line 3 of claim 5, the phrase "the liquid reagent" should be changed to --the mixture-- since it is the mixture in part b) whose temperature is determined.

Claim 9 is indefinite since it is not understood how the prothrombin time is obtained from a table with rows and columns since independent claim 1, from which claim 9 depends, recites that the prothrombin time is obtained from the equation for INR.

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 1-3, 5-7 and 10-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Applicant's admitted prior art on pages 1-2 of the instant specification in view of Zweig (WO 93/22453, submitted in the IDS filed on December 14, 2005).

Applicant admits on pages 1-2 of the instant specification that it is known in the prior art to perform a prothrombin time test on a blood sample at 37^0C by combining a blood sample with liquid thromboplastin reagents and determining the time needed for the mixture to clot. The prothrombin time is expressed as an International Normalized Ratio (INR). Applicant admits that the equation for determining INR equals the ratio between the clotting time (CT) of a test sample and the normal clotting time (NCT) of a sample from an average normal individual raised to the power of the International Sensitivity Index (ISI) (i.e. $INR=(CT/NCT)^{ISI}$). Applicant also admits that in an Owren-type PT test, it is known to include in the PT reagent a sufficient amount of fibrinogen to increase the fibrinogen content of the mixture of sample and reagent by at least 0.1 g/L, and that the relationship between reagent and sample in an Owren-type PT test is greater than four. Applicant admits that known, prior art PT tests are commonly performed at 37^0C in order to mimic the physiological situation. However, this requires that some sort of thermostat/heating means be present in the device for measuring prothrombin time in order to maintain a temperature of 37^0C. See pages 1-2 of the instant specification. Applicant fails to teach that a prothrombin time test can be performed at an ambient room temperature of between 15-45^0C, and that the measured ambient temperature can be used in the measurement of the prothrombin time calculated using the known INR equation in order to compensate for the temperature at which the test was performed.

Zweig teaches of a test article and a method for performing a blood coagulation assay such as prothrombin time. Zweig teaches that the blood coagulation test can be performed at room temperatures thereby eliminating the need for elaborate temperature control means. The coagulation apparatus taught by Zweig comprises a control circuitry which includes a temperature measurement capability so that variations in temperature can be taken into account when interpreting the test results. The circuitry further includes calculating means for calculating the coagulation value of blood. Zweig teaches that if the prothrombin time test is performed at ambient temperature, the temperature of the sample and reagent is determined by a temperature recording means such as a thermocouple, and the PT time is adjusted accordingly. Therefore, the circuitry includes a temperature adjustment algorithm that compensates the measured prothrombin time for temperature. In other words, the initially determined coagulation value is adjusted upwards or downwards to compensate for variations in the sample temperature that is at ambient temperature different from the standard 37^0C. See lines 3-15 on page 6, lines 9-28 on page 16 and lines 1-26 on page 17 of Zweig.

Based upon the combination of Applicant's admitted prior art and Zweig, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to perform the prothrombin time test taught as known by Applicant on pages 1-2 of the instant specification at an ambient room temperature of between 15-45^{0}C, and to use the measured ambient temperature in the calculation of the prothrombin time by the known INR equation since Applicant admits that it is cumbersome to perform the known prothrombin time test at 37^0C since this requires a thermostat/heating means, and Zweig teaches that prothrombin time tests can be performed at ambient temperatures lower than 37^0C by simply measuring the temperature of a sample/reagent

mixture in the range of an ambient/room temperature, and incorporating this measurement into the calculation of the prothrombin time using some sort of temperature adjustment algorithm that serves to temperature compensate the PT coagulation value. It also would have been obvious to one of ordinary skill in the art to incorporate the components needed to perform the known prothrombin time test taught by Applicant in the specification, including a vessel containing liquid reagents for clotting a blood sample and a timing means for measuring the time required for a sample combined with the reagents to coagulate, into a kit form so as to provide a single use packaged device to a user in a ready-to-use form for the performance of a point-of-care prothrombin test that is quick and easy to use by having all of the required materials needed to perform the test in one location. It would have been obvious to one of ordinary skill in the art to include a temperature recording means in the kit of the prothrombin time test taught by Applicant for the purpose of measuring the ambient temperature of the sample being tested in accordance with the teaching of Zweig to perform prothrombin time tests at ambient temperatures and to temperature compensate the measured prothrombin values. It also would have been obvious to one of ordinary skill in the art to include a volume determining means in the kit of the prothrombin time test taught by Applicant for the purpose of measuring the amount of blood tested and the amount of blood that coagulates during the test.

6. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Applicant's admitted prior art on pages 1-2 of the specification in view of Zweig as applied to claims 1-3, 5-7 and 10-14 above, and further in view of Moyer et al (US 3,951,606, submitted in the IDS filed on December 14, 2005). For a teaching of Applicant's admitted prior art and Zweig, see previous paragraphs in this Office action. Applicant and Zweig fail to teach that the prothrombin time

can be obtained from a table with rows and columns where one is for clotting times and the other is for various temperatures.

Moyer et al teach of a method and apparatus used for prothrombin testing on a blood sample. The apparatus comprises a uniform bore reaction tube or vessel containing therein liquid reagents for clotting a blood or plasma sample that have been lyophilized. The liquid reagents include thromboplastin and other additives for clotting blood. The tube contains calibration marks thereon that serve to indicate the volume of sample in the tube (i.e. the calibration marks serve as a volume determining means). To use the device to perform a prothrombin test, a sample of whole blood or plasma is obtained from a finger puncture, and the blood is added to the top of the tube. The sample of blood descends in the tube, thereby contacting the dried coagulation reagents. The sample continues to descend in the tube until the time at which a clot forms that serves to stop any further movement of the sample in the tube. Moyer et al teach that prothrombin times are normally obtained at a temperature of 37^0C. However, Moyer et al teach that using the reaction tube described, a prothrombin time test can be performed at room temperature provided a calibration plot is constructed which relates the two sets of data (i.e. the standard prothrombin times obtained at 37^0C, and prothrombin times obtained at a room temperature of about 22-23^0C). Therefore, the method taught by Moyer et al includes the steps of mixing in a vessel a sample of blood with reagents that become liquid upon combination with a blood sample, determining the room temperature of the mixture in the range of about 22-23^0C, determining the clotting time of the sample that correlates to the distance of the downward travel of the sample in the vessel before coagulation, and calculating the prothrombin time of the blood sample based upon both the measured clotting time and the temperature of the sample. The

prothrombin time of the sample is determined by using a calibration table of rows and columns where one of the rows and columns includes clotting times, and the other of the rows and columns includes temperatures such as 22^0C, 23^0C and 37^0C. The clotting time of the sample measured at an ambient temperature of 22-23^0C is compared to the clotting time of a sample measured at 37^0C using the same apparatus in order to determine the prothrombin time of the blood sample. Therefore, the prothrombin time of a blood sample is determined in the method and apparatus taught by Moyer et al using both a determination of the temperature and the clotting time of the sample. See Figures 1-2, the abstract, lines 33-51 in column 2, lines 35-60 in column 4, lines 1-15 and 41-62 in column 5, lines 25-51 in column 6 and the claims in Moyer et al.

Based upon the combination of Applicant's admitted prior art, Zweig and Moyer et al, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to perform the prothrombin time test taught as known by Applicant on pages 1-2 of the instant specification at an ambient room temperature of between 15-45^0C, and to use the measured ambient temperature in the determination of the prothrombin time by using a table with rows and columns where one is for clotting times and the other is for various temperatures since Moyer et al teach of determining the prothrombin time of a blood sample using both a determination of the temperature and the clotting time of a sample, and then finding the prothrombin time from a calibration table of rows and columns representing both different clotting times at different temperatures.

7. Claims 10 and 12-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moyer et al (US 3,951,606). For a teaching of Moyer et al, see previous paragraphs in this Office action.

Moyer et al fail to teach that the apparatus for determining prothrombin time of a blood sample can be incorporated into a kit including a vessel having lyophilized coagulation reagents therein, a temperature recording means, a time registration means and a volume determining means. However, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the apparatus taught by Moyer et al including a vessel having lyophilized coagulation reagents therein and a volume determining means (i.e. calibration marks) into a kit so as to provide a single use packaged device to a user in a ready-to-use form for the performance of a point-of-care prothrombin test that is quick and easy to use by having all of the required materials needed to perform the test in one location. It also would have been obvious to one of ordinary skill in the art to include a temperature recording means in the apparatus taught by Moyer et al since Moyer et al disclose the performance of the prothrombin test at a temperature other than the standard 37^0C, such as room temperatures of about 22-23^0C, and thus a temperature recording means would serve to measure the exact temperature at which the test is being performed. It also would have been obvious to one of ordinary skill in the art to incorporate a time registration means in the apparatus taught by Moyer et al so as to provide a simple measurement of the time it takes a blood sample added to the tube to coagulate without having to rely on the measurement of the distance traveled in the tube by the blood sample.

8. Applicant's arguments with respect to claims 1-3, 5-7 and 9-14 have been considered but are moot in view of the new ground(s) of rejection.

The previous objection to the abstract made in the last Office action mailed on July 1, 2008 has been withdrawn in view of the amendments made to the abstract. In addition, the previous rejections of the claims under 35 USC 112, second paragraph made in the last Office action have been withdrawn in view of Applicant's amendments to the claims. However, new rejections of the amended claims under this statute are set forth above, as necessitated by the amendments made to the claims. The previous rejection of the claims under 35 USC 102(b) as being anticipated by Moyer et al has been withdrawn in view of the amendments made to the claims.

The previous rejections of the claims under 35 USC 103 as being obvious over Moyer et al and over Applicant's admitted prior art in view of Zweig have been maintained and modified as set forth above. Amended claim 1, which now incorporates previously allowable claim 8, is newly rejected under 35 USC 103 as being obvious over Applicant's admitted prior art in view of Zweig since Applicant admits on page 2 of the specification that it is known to calculate the prothrombin time of a blood sample by solving the known equation for INR that equals the ratio between the clotting time (CT) of a test sample and the normal clotting time (NCT) of a sample from an average normal individual raised to the power of the International Sensitivity Index (ISI) (i.e. $INR=(CT/NCT)^{ISI}$). Based upon the combination of Applicant's admitted prior art and Zweig, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to perform the prothrombin time test taught as known by Applicant on pages 1-2 of the instant specification at an ambient room temperature of between 15-45^{0}C, and to use the measured ambient temperature in the calculation of the prothrombin time by the known INR equation since Applicant admits that it is cumbersome to perform the known prothrombin time

test at 37^0C since this requires a thermostat/heating means, and Zweig teaches that prothrombin time tests can be performed at ambient temperatures lower than 37^0C by simply measuring the temperature of a sample/reagent mixture in the range of an ambient/room temperature, and incorporating this measurement into the calculation of the prothrombin time using some sort of temperature adjustment algorithm that serves to temperature compensate the PT coagulation value.

Since this Office action introduces a new ground of rejection that could have been applied to previous claim 8, and claim 8 is now incorporated into claim 1, it is not being made final.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maureen M. Wallenhorst whose telephone number is 571-272-1266. The examiner can normally be reached on Monday-Thursday from 6:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden, can be reached on 571-272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maureen M. Wallenhorst
Primary Examiner
Art Unit 1797

mmw

October 23, 2008

/Maureen M. Wallenhorst/

Primary Examiner, Art Unit 1797